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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 02/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/661,005	BULOW ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 11/16/2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 08/15/2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 11/16/2005, claims 1-17 are pending in the application.

New Objections/Rejections

Claim Objections

Claim 15 is objected to because of the following informalities: Claim 15 recites "wherein one or more the cells..." The sentence is not grammatically correct because it appears to lack a preposition. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 recites the phrase "exposing the cells to a potential drug". It is unclear at what point the cells would be exposed to "a potential drug." Claim 1 is drawn to a method wherein the siRNA is immobilized on a support, the cells are then plated on said support and detecting of the biological effect of the siRNA on the cell occurs. Claim 9 is further limiting by reciting the method further comprises exposing the cells to a potential drug. When does this occur: before the cells are plated on the support, after the cells have been plated on the support, before the cells are detected for the biological effect of the siRNA or after the cells have been detected for the biological effect of the siRNA on the cells?

Additionally, the phrase "a potential drug" is not defined by the claim and the specification does not provide any information on what a potential drug could be and therefore the claim is indefinite for failing to particularly pointing out what applicant regards as the invention.

Claim Rejections - 35 USC § 102

For prior art purpose, "a potential drug" is being interpreted to mean any substance. Merriam Webster's dictionary (5th Ed. 1997) defines potential to mean "something that can develop or become actual" (see page 573) and further defines drug as "a substance used as or in medicine" (see page 238). Therefore, a potential drug is being interpreted to mean any substance that can develop or become a drug used as or in medicine.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-2, 4-6, 7-12 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Caplen et al. (WO 03/012052).

The instant claims are drawn to a method for investigating the biological effect of a siRNA directed against one gene present in a cell comprising providing a support comprising on pre-determined locations thereon at least one siRNA species immobilized on said support, plating cells on a support, adding the siRNA and detecting the biological effect of the siRNA on the cells and further wherein the siRNA is obtained by chemical synthesis at the predetermined locations on the surface of the support, wherein the double stranded nucleotides are RNA corresponding to a partial or completed coding sequence of the corresponding genes, wherein the support is selected from a group as listed and the locations for the siRNA are isolated by a physical barrier, wherein the detection of the biological effect is determined.

Caplen et al. teach a cell based gene silencing method comprising immobilizing siRNA onto the surface of a solid support wherein the support is a glass slide, a chamber slide, a culture plate or a 96-well titer plate (see page 26, lines 15-16) wherein the siRNA are directed against at least one gene present in the cell, plating cell on the support containing said siRNA and detecting

the biological effect of the siRNA on the cells. Further, Caplen et al. teach exposing cells to OptiMEM medium, FBS and G418 before being plated on the support and treated with OptiMEM medium and FBS after being plated on the support (see page 57, lines 1-24).

Thus, Caplen et al. anticipates claims 1-2, 4-6, 7-12 and 14 of the instant application.

Claims 1-2, 4-6, 7-12 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Mittal et al. (U.S. 2005/0042641).

The instant claims are drawn to a method for investigating the biological effect of a siRNA directed against one gene present in a cell comprising providing a support comprising on pre-determined locations thereon at least one siRNA species immobilized on said support, plating cells on a support, adding the siRNA and detecting the biological effect of the siRNA on the cells and further wherein the siRNA is obtained by chemical synthesis at the predetermined locations on the surface of the support, wherein the double stranded nucleotides are RNA corresponding to a partial or completed coding sequence of the corresponding genes, wherein the support is selected from a group as listed and the locations for the siRNA are isolated by a physical barrier, wherein the detection of the biological effect is determined by cell division, proliferation, differentiation or apoptosis and further the proteins of the cells are analyzed by western analysis, northern blot analysis or RT-PCR analysis.

Mittal et al. teach a method of determining the biological effect of siRNA targeted against at least one gene present in a cell comprising immobilizing chemically synthesized siRNA onto discreet, defined locations into the wells of a microtiter plate, plating cells on the

surface of the plate allowing the siRNA to enter the cell and detecting the biological effect of the siRNA on the cells (see paragraph 0011).

Thus, Mittal et al. anticipates claims 1-2, 4-6, 7-12 and 14 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caplen et al. (WO 03/012052) as applied to claims 1-2, 4-6, 7-12 and 14 above, and further in view of Myers et al. (Nature Biotechnology, 2003, Vol. 21: 324-328) and Yang et al. (PNAS 2002, Vol. 99 (15): 9942-9947.

The instant claims are drawn to a method for investigating the biological effect of a siRNA directed against one gene present in a cell comprising providing a support comprising on pre-determined locations thereon at least one siRNA species immobilized on said support, plating cells on a support, adding the siRNA and detecting the biological effect of the siRNA on the cells and further wherein the siRNA is obtained by enzymatic digestion, by dicer or RNase III-type enzymes, of double stranded nucleotides or by chemical synthesis at the predetermined locations on the surface of the support, wherein the double stranded nucleotides are RNA corresponding to a partial or completed coding sequence of the corresponding genes, wherein the

support is selected from a group as listed and the locations for the siRNA are isolated by a physical barrier, wherein the detection of the biological effect is determined.

Caplen et al. teach a cell based gene silencing method comprising immobilizing siRNA onto the surface of a solid support wherein the support is a glass slide, a chamber slide, a culture plate or a 96-well titer plate (see page 26, lines 15-16) wherein the siRNA are directed against at least one gene present in the cell, plating cell on the support containing said siRNA and detecting the biological effect of the siRNA on the cells. Further, Caplen et al. teach the cells were exposed to OptiMEM medium, FBS and G418 before being plated on the support and treated with OptiMEM medium and FBS after being plated on the support (see page 57, lines 1-24). Caplen et al. does not teach the siRNA is obtained by Dicer.

Myers et al. teach generation of siRNA by enzymatic digestion of long dsRNA using Dicer. Yang et al. teach similar generation of siRNA by enzymatic digestion of long dsRNA using RNase III.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to enzymatically digest long dsRNA into siRNA, as taught by Myers et al. and Yang et al., for use in analysis of mammalian gene function.

One would have been motivated to use siRNA generated by enzymatic digestion of long dsRNA instead of synthetic siRNA to analyze gene function because siRNA made synthetically may not be very functional and several siRNA need to be tried against a target before a particular gene is successfully silenced and therefore siRNA would not be suitable for use in a library to screen for the biological effects of siRNA on a particular gene in a cell (see Myers et al. page 324). Yang et al. teach a similar advantage for using siRNA generated by enzymatic digestion of

long dsRNA and in a screening assay for determining the biological effects of siRNA on gene function, one of skill in the art would be motivated to make the most functional siRNA for efficient gene silencing (see page 9947). Further, one would have been motivated to use siRNA generated by enzymatic digestion because synthetic siRNA are very expensive to make and enzymatically obtained siRNA are an inexpensive, efficient method for generating an effective pool of siRNA capable of silencing gene expression in cells (see Myers et al. page 325).

Because Caplen et al. demonstrated an effective method for analyzing the biological effect of cells transfected by synthetic siRNA immobilized on a support, one would have a reasonable expectation of success using siRNA generated by enzymatic digestion because Myers et al. teach functional and specific siRNA generated by enzymatic digestion of dsRNA using Dicer and Yang et al. teach siRNA generated by enzymatic digestion of dsRNA using RNase III can silence gene expression in mammalian cells.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments/Amendments

Applicant's arguments are moot in view of Applicant's claim amendments filed 11/16/2005 and new grounds of rejections above.

Re: Claim Rejections - 35 USC § 112

The rejection of record of claims 9 and 13-15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention is withdrawn in response to Applicant's claim amendments filed 11/16/2005.

Re: Claim Rejections - 35 USC § 102

The rejection of record of claims 1-6, 8-11 and 12-13 under 35 U.S.C. 102(b) as being anticipated by Harborth et al. (Journal of Cell, 2001), Caplen et al. (Gene, 2000), McManus et al. (RNA, 2002), Fosnaugh et al. (US 2003/0148507) and Tzertzinis et al. (US 2004/0038278) are withdrawn in response to Applicant's amendments filed 11/16/2005.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong
Examiner
Art Unit 1635